



WARWICK

CLINICAL TRIALS UNIT



optimabreaststudy.com

Optimal Personalised Treatment of early breast cancer using Multi-parameter Analysis

Chief Investigator: Professor Rob Stein (UCL Hospitals)

OPTIMA trial organisation



Funder: National Institute for Health Research (NIHR) Health Technology Assessment Programme Health Technology Assessment (HTA) Programme



Sponsor: University College London



Trial Coordination: Warwick Clinical Trials Unit, University of Warwick



Qualitative Recruitment Study: University of Bristol



University of
BRISTOL

Why do the OPTIMA trial?

- Adjuvant chemotherapy is currently standard practice for patients with ER+ve HER2-ve node positive early breast cancer.
- Many of these patients may gain little extra benefit from chemotherapy in addition to hormonal treatment.
- These patients cannot be reliably identified by conventional pathology.
- Multi-parameter tests may be able predict which patients are likely to benefit from chemotherapy.
- Current evidence is not good enough to safely change clinical practise.
- OPTIMA aims to prove this and hence allow many patients to avoid chemotherapy safely.

OPTIMA and COVID-19

- Breast cancer patients still need high-quality treatment and we still need to generate knowledge to improve treatment despite COVID.
- Adopting test-guided chemotherapy for patients with node-positive disease without proof of efficacy places patients at risk.
- OPTIMA is even more relevant because of the pandemic.
- De-escalation trials allow patients to be treated less intensively in a controlled framework.
- The OPTIMA trial has remained open to recruitment throughout the COVID-19 pandemic as a priority clinical trial.
- OPTIMA allows one third of participants who would be normally treated with chemotherapy to avoid this, reducing patient risk from treatment and from hospital visits.

OPTIMA prelim

Feasibility study

Before embarking on the main OPTIMA study we successfully completed a feasibility study.

- 412 patients were randomised into OPTIMA prelim.
- Chemotherapy decisions were made using Oncotype DX.
 - The test was performed by (Exact Sciences/) Genomic Health Inc. in California.

OPTIMA prelim:

- Demonstrated that the main OPTIMA study was acceptable to patients and clinicians.
- Informed the choice of Prosigna as the main trial test technology for chemotherapy decisions.

About multi-parameter assays

- Multi-parameter assays provide information about tumour biology that is more reliable than tumour grade.
 - Think of as providing a molecular grade.
- Six different tests are widely available in Europe & N. America – there is no gold standard!
- Tests provide information about risk of recurrence:
 - Superior to tumour grade for node-negative breast cancer.
 - Work best when combined with clinical data – tumour size & nodal status.
- NICE approved the Prosigna, EndoPredict and Oncotype DX tests to assist chemotherapy decisions for patients without lymph node involvement (DG34 guidelines, December 2018)
 - The main OPTIMA trial uses Prosigna.
- The tests may also predict chemotherapy sensitivity. This is the OPTIMA hypothesis.

What is Prosigna?

WARWICK

CLINICAL TRIALS UNIT

- Test measures expression of 50 genes (PAM50 gene set)
- Uses specialised equipment – highly reliable and reproducible – can be performed in any suitably qualified pathology laboratory.
- Prosigna provides:
 - A numerical “Risk of Recurrence” (ROR) score – predicts 10 year risk of metastatic relapse.
 - Intrinsic subtype (luminal A, luminal B, Her2-enriched or basal-like).
- Subtype adds information to ROR score.
 - Almost all ER+ve HER2-ve breast cancers are luminal A/B.
 - About 3-5% are non-luminal – these may be less sensitive to hormone therapy

Prosigna® Breast Cancer Prognostic Gene Signature Assay



INFORMATION SHEET

- Prosigna is a tumour gene expression signature test. It uses the “PAM50” gene set to generate individualised prognostic information.
- The test can be performed by accredited laboratories in the UK.
- Prosigna provides an estimate of a patient’s 10-year risk of distant recurrence and assigns the cancer to an intrinsic subtype (Luminal A, Luminal B, Her2-Enriched, or Basal-like).
- It is approved by NICE to assist chemotherapy decisions for patients with “intermediate risk” node-negative ER+ve HER2-ve tumours.

There is a trial information sheet on Prosigna which gives more detail about the test. You can find this in your Investigator Site File.

Why Prosigna?

Evaluation of alternative multi-parameter tests

- OPTIMA prelim used Oncotype DX to make chemotherapy decisions
 - 6 tests (including Oncotype) were compared in OPTIMA prelim
 - All the tests were shown to provide broadly equivalent risk information for the population
- Prosigna was chosen for the OPTIMA main trial because:
 - Very well validated as prognostic test
 - Can be performed in NHS labs (no overseas samples)
 - Health economics analysis suggests modestly more cost effective than others
- In OPTIMA prelim 18% of tumours had a “high score” (>25) by Oncotype DX vs. 34% by Prosigna
 - Patients with high-score tumours are allocated chemotherapy
 - Prosigna is the more conservative test
 - This may be important in node-positive breast cancer

OPTIMA Trial hypothesis

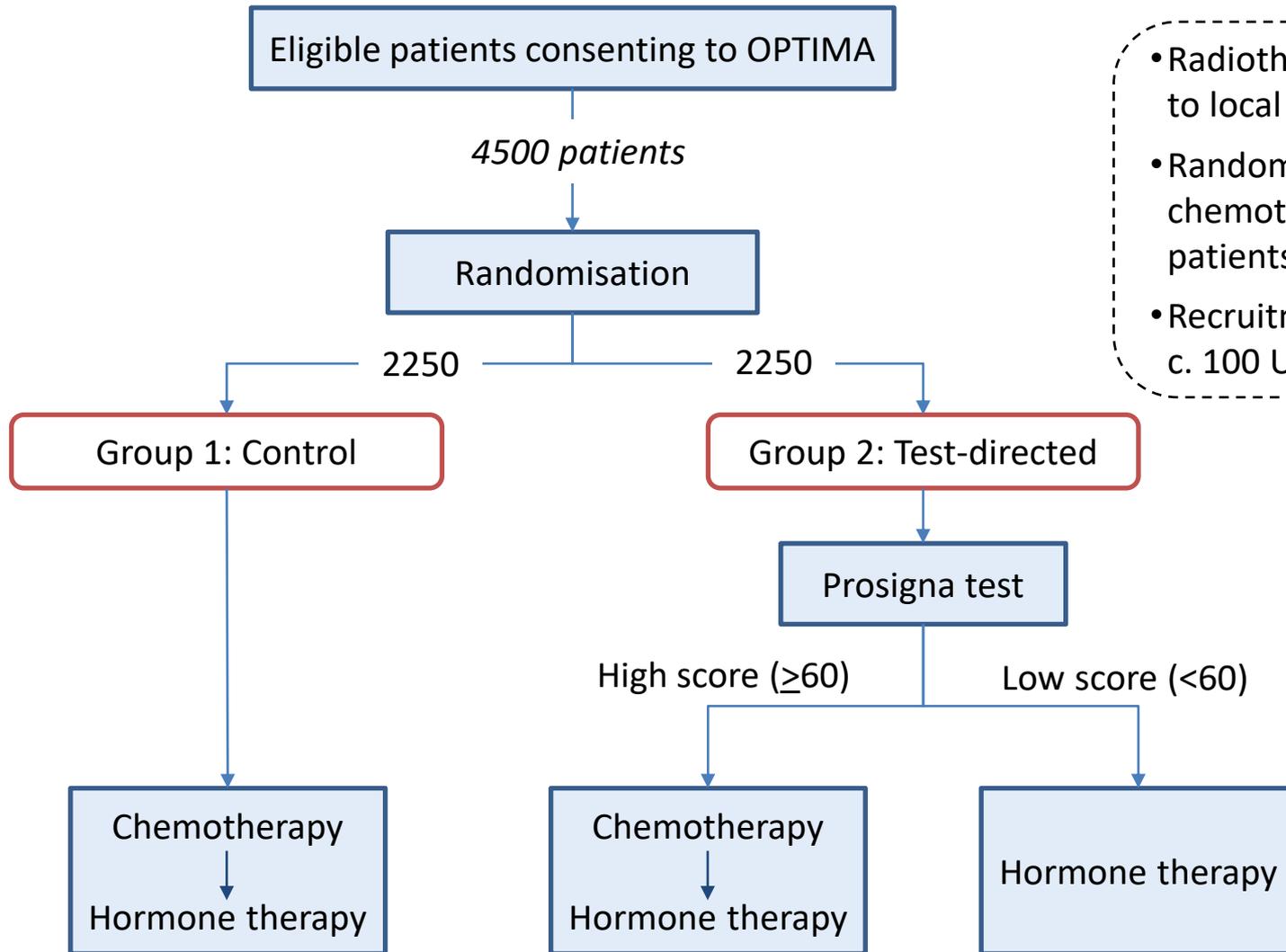
Tumour multi-parameter assays predict chemotherapy sensitivity.

Patients with hormone sensitive primary breast cancers that have a low multi-parameter assay score do not have a meaningful chance of benefiting from adjuvant chemotherapy despite other factors that may predict for a high risk of disease recurrence.

Trial objectives

- To identify a method of selection that reduces chemotherapy use for patients with hormone sensitive primary breast cancer without detriment to recurrence and survival.
- To establish the cost-effectiveness of test-directed treatment strategies compared to standard practice

Trial design



- Radiotherapy given according to local practice in both groups.
- Randomisation blinded for chemotherapy assigned patients.
- Recruitment over 5 years from c. 100 UK sites.

Primary outcome measures

- Invasive Disease Free Survival (IDFS): non-inferiority of test-directed chemotherapy treatment and endocrine therapy compared to chemotherapy followed by endocrine treatment
IDFS includes all loco-regional recurrence of invasive breast cancer, contralateral new invasive breast cancer, metastatic disease, death from breast cancer, death from all other causes & new non-breast cancer
- Cost effectiveness evaluation of protocol specified multi-parametric assay driven treatment against standard clinical practice

Secondary outcome measures

- Invasive Disease Free Survival for patients with low-score tumours
- Distant Recurrence Free Interval (DRFI) and Distant Recurrence Free Survival (DRFS)
- Breast Cancer Specific Survival (BCSS) and Overall Survival (OS)
- Health Resource Use and Quality of Life as measured by EQ-5D and FACT-B
- Patient compliance with long-term endocrine therapy

Inclusion criteria

- ✓ Female or male age ≥ 40
- ✓ Excised invasive breast cancer
- ✓ ER positive with $>10\%$ staining and HER2 negative
- ✓ Tumour size and axillary lymph node status of either:
 - ✓ 4-9 lymph nodes involved AND with any invasive tumour size
 - ✓ 1-3 nodes involved, at least 1 nodes containing a macrometastasis (i.e. deposit $>2\text{mm}$ diameter) AND with any invasive tumour size
 - ✓ 1-3 lymph nodes involved with micrometastases only (i.e. deposit $>0.2\text{-}2\text{mm}$ diameter) AND invasive tumour size $\geq 20\text{mm}$
 - ✓ Node negative AND tumour size $\geq 30\text{mm}$

Note: Nodes containing isolated tumour cell clusters (ITC) only (i.e. deposit $\leq 0.2\text{mm}$ diameter) will be considered to be uninvolved.

Note: Involvement of lymph nodes with macrometastases or micrometastases may be determined either by histological examination or by OSNA or equivalent PCR-based assay.

Inclusion criteria

- ✓ Considered appropriate for adjuvant chemotherapy by the treating physician.
- ✓ Patient must be fit to receive chemotherapy and other trial-specified treatments with no concomitant medical, psychiatric or social problems that might interfere with informed consent, treatment compliance or follow up.
- ✓ Multiple ipsilateral cancers are permitted provided at least one tumour fulfils the tumour size and axillary node entry criteria and none meet any of the exclusion criteria.

NOTE: refer to section 10.2 of the protocol for guidance on selection of tumour blocks to be sent to the Central Laboratory

Inclusion criteria

- ✓ Bilateral cancers are permitted provided the tumour(s) in one breast meets the eligibility criteria and the contralateral tumour is not ER negative/ low-positive ($\leq 10\%$ staining) and/or HER2 negative and is not clinically significant, defined by both of the following:
 - i. The contralateral tumour does not meet the tumour size and lymph node eligibility criteria for trial entry, i.e. the following are not acceptable: presence of lymph node macro-metastases; presence of lymph node micrometastases if tumour size $\geq 20\text{mm}$; tumour size $\geq 30\text{mm}$ if no lymph node involvement.
 - ii. The treating physician does not consider that the characteristics of the contralateral tumour alone justify consideration of adjuvant chemotherapy.
- ✓ Short term pre-surgical treatment with endocrine therapy including in combination with non-cytotoxic agents is allowed providing that the duration of treatment does not exceed 8 weeks.

NOTE: a pre-treatment core biopsy should be sent to the Central Laboratory; a sample from a surgical excision or other on-treatment biopsy is not acceptable. Further guidance in section 10.2 of the protocol
- ✓ Informed consent for the study

Exclusion criteria

WARWICK

CLINICAL TRIALS UNIT

X ≥ 10 involved axillary nodes or evidence for internal mammary node involvement.

NOTE - Internal mammary lymph nodes identified by anatomical imaging studies alone will be considered uninvolved where the diameter is $< 10\text{mm}$.

X ER negative / low-positive OR HER2 positive/amplified.

X Metastatic disease. *NOTE – Formal staging according to local protocol is recommended for patients where there is a clinical suspicion of metastatic disease or for stage III disease (tumour $> 50\text{mm}$ with any nodal involvement OR any tumour size with 4 or more involved nodes).*

X Previous diagnosis of malignancy unless:

- Managed only by surgical treatment with or without local radiotherapy AND disease-free for 10 years
- basal cell carcinoma of skin or cervical intraepithelial neoplasia
- ductal carcinoma in situ (DCIS) or pleomorphic lobular carcinoma in situ (pleomorphic LCIS) of the breast treated with surgery with or without breast radiotherapy; treatment with anti-oestrogens is not permitted.

NOTE: Isolated classical type lobular carcinoma in situ (LCIS) is not considered in this context to be a diagnosis of malignancy.

Exclusion criteria

WARWICK

CLINICAL TRIALS UNIT

- X Pre-operative anti-cancer treatments except short-term endocrine therapy administered as per the inclusion criteria.
- X Adjuvant systemic treatment commenced prior to trial entry* except endocrine therapy, which must be discontinued prior to starting trial-allocated chemotherapy.
- X Treatment with agents, including ovarian suppression, known to influence breast cancer growth but prescribed for other indications within one year of trial entry* except as follows
 - i. Use of oestrogen replacement therapy (HRT) provided this is stopped before surgery.
 - ii. Drugs administered for *in vitro* fertilization or fertility preservation.
 - iii. Use of hormonal contraception.

*Trial entry is defined as the date of informed consent.

Exclusion criteria

WARWICK

CLINICAL TRIALS UNIT

- X Trial entry* and randomisation more than 12 weeks after completion of breast cancer surgery. Trial entry should ordinarily be within 8 weeks of final surgery.
*Trial entry is defined as the date of informed consent.
- X Planned further surgery for breast cancer, including axillary surgery, to take place after randomisation, except either re-excision or completion mastectomy for close or positive/involved margins which may be undertaken following completion of chemotherapy if given.

NOTE: The timing of radiotherapy to the axilla for lymph-node involvement is not restricted.

Understanding the ER eligibility criteria

WARWICK

CLINICAL TRIALS UNIT

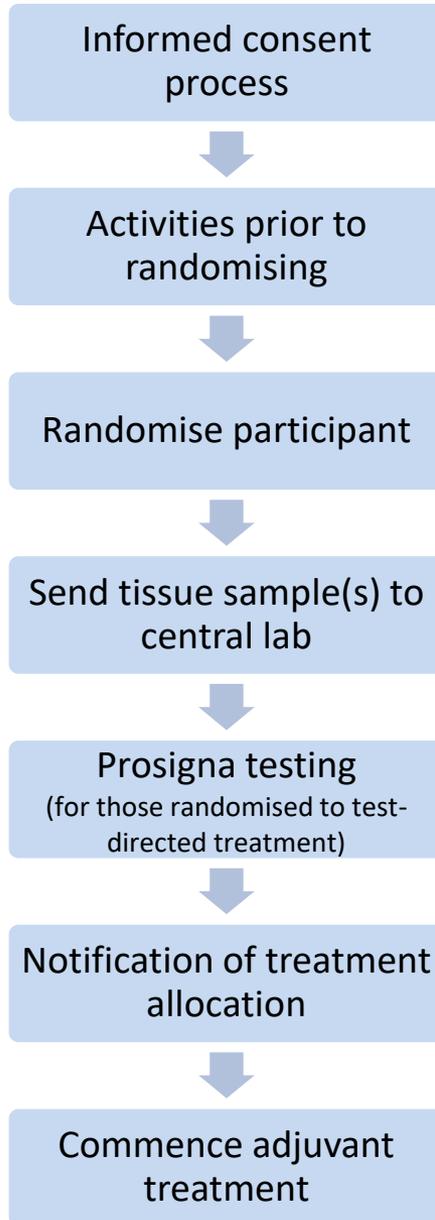
- OPTIMA excludes ER low-positive tumours, defined as having 1-10% +ve staining.
- There are several methods of reporting ER status. Allred (or Quick) Score and H-Score combine %staining and staining intensity

Understanding Allred score

Add	% staining	0.1%-1%	>1%-10%	>10%-33%	>33%-67%	>67%-100%
	score	1	2	3	4	5
Add	Staining intensity	weak	moderate	strong	Result = 0 or 2-8	
	score	1	2	3		

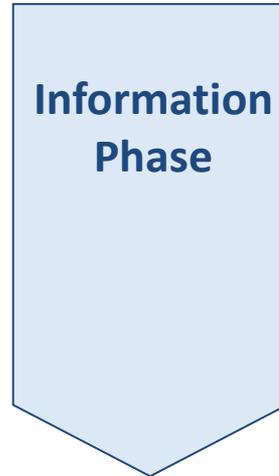
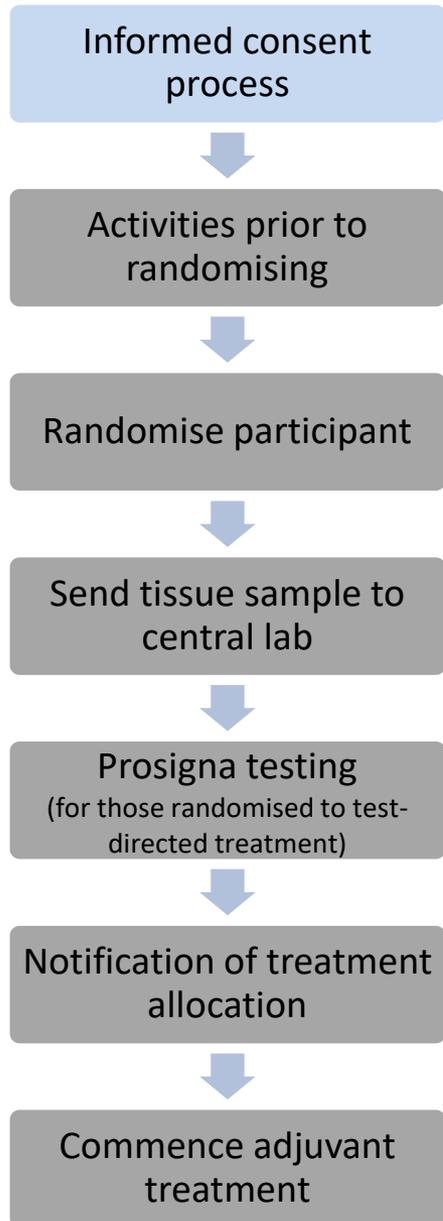
- All tumours with an Allred Score of 3 or less are ineligible. All tumours with scores 6-8 are eligible but for scores 4 or 5, you need to know %staining for eligibility.
- We are now asking sites to report %staining for all tumours

Patient pathway



- Patients usually approached at first oncology consultation.
- Avoid giving patients pre-conceptions about their adjuvant treatment, as these perceptions can be difficult to overcome once made.
- Promote awareness amongst local team that site participating in OPTIMA.
- Preliminary information sources for potential participants
 - Patient Flyer & Clinic Poster
 - OPTIMA website: optimabreaststudy.com

Informed consent – information phase



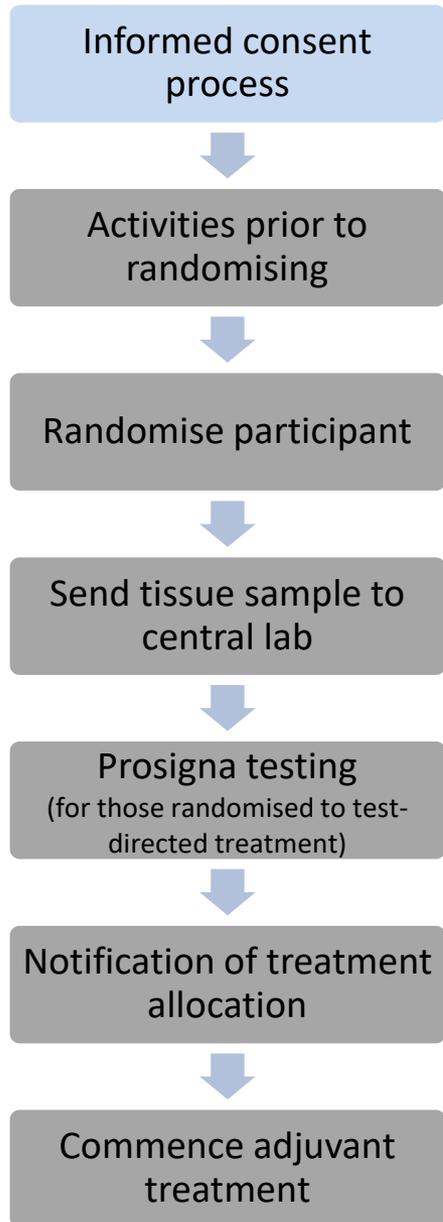
- Confirm eligibility
- Approach potential participant in clinic or during telephone or video consultation
- Discuss study in detail
- Provide patient with written information sheet in person or by post / email
 - PIS may be sent out in advance of consultation.
- Opportunity for questions



TIME FOR CONSIDERATION
(Recommendation is at least 24hrs)



Consenting phase



Information
Phase

Time

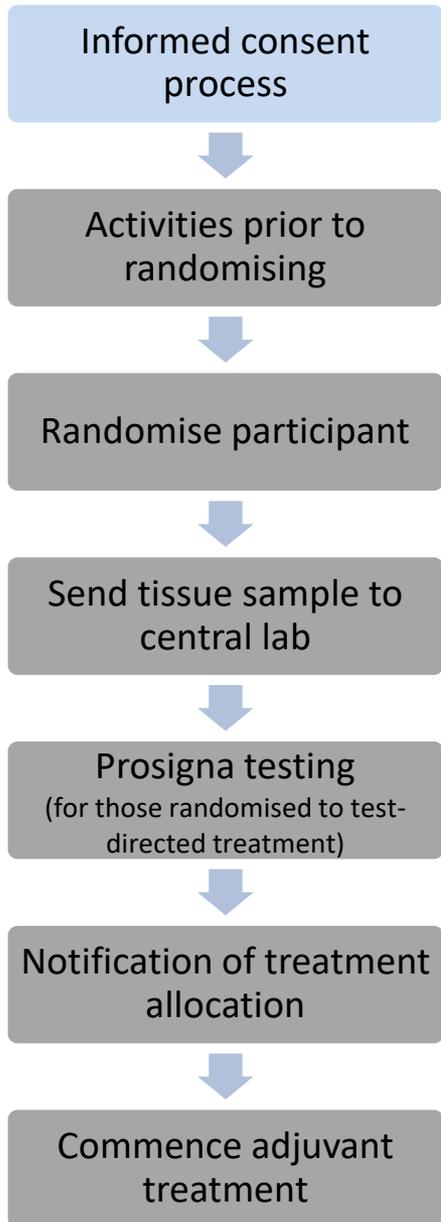
Consenting
Phase

ALLOW TIME FOR CONSIDERATION
(Recommendation is at least 24hrs)

- Answer any further questions
- Participant initials each item on the **consent form**, signs & date.
- Participant may complete the CF in clinic **OR** remotely.
 - If CF is completed remotely, participant takes original to clinic or sends by post to named individual.
 - Alternatively participant may scan/ photograph CF and send electronically e.g. to approved email.
- Investigator* countersigns & dates the **consent form**.
 - Specific procedure for countersigning a photographic copy of consent form – refer to protocol.
- In all cases, investigator who countersigns the consent form must be satisfied that consent is genuine.

*PI/or designee with *consent role assigned in the Delegation Log*

Remote verbal consent



Information Phase

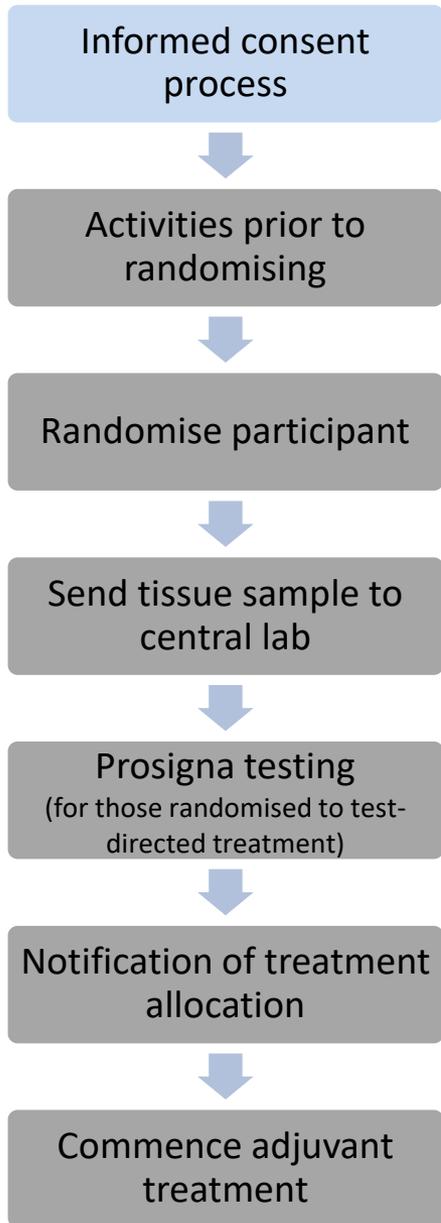
Time

Consenting Phase

- Allows participant to give initial **verbal consent during telephone or video consultation** for convenience, e.g. to avoid delays.
- **Limited scope:** allows randomisation and completion of pre-treatment allocation processes only.
 - Answer any further questions.
 - Participant states intention to join study.
 - Investigator* identifies likely delay in completion of written consent process and offers verbal consent; participant agrees.
 - Investigator* completes the Documentation of Remote Verbal Consent form.
 - Once written consent has been received, this should be countersigned whenever possible by the investigator who received verbal consent.

*PI/or designee with *consent role assigned in the Delegation Log*

Processing consent



Information Phase

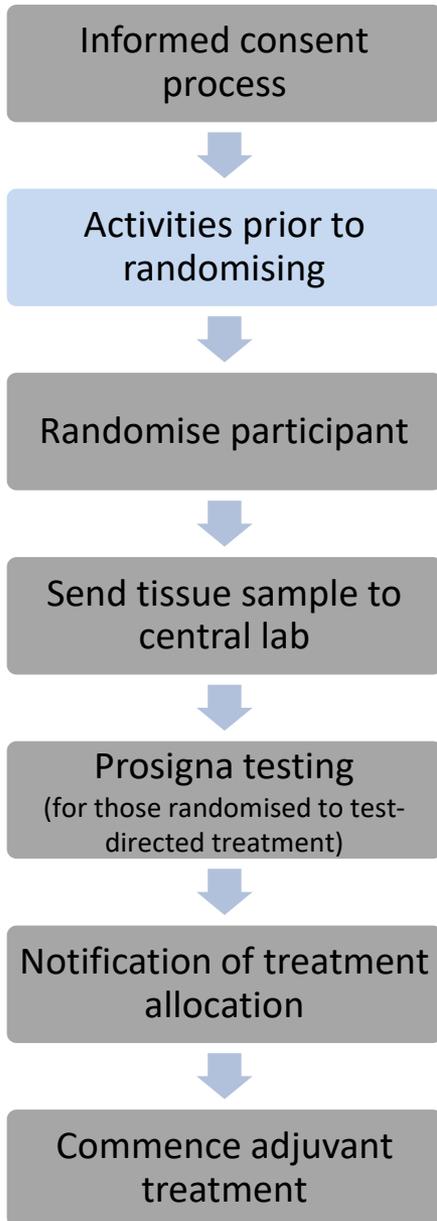
Time

Consenting Phase

Processing Consent

- The original signed & dated consent form should be filed in the Investigator Site File.
- The Documentation of Remote Verbal Consent form should also be filed in the Investigator Site File if relevant.
- Copies (paper or electronic) of all consent documents must be given/ sent to patient.
- Patient participation must be recorded in medical notes.
- Send GP letter.
- **Consent forms must not be sent to Trial Office**

Before randomisation



✓ Confirm eligibility	Complete <i>Eligibility Form (CRF 1)</i>
✓ Obtain Informed Consent	Complete the appropriate <i>Consent Form</i> (as per previous slides)
✓ Confirm stratification information	Complete <i>Randomisation Form (CRF 2)</i>
✓ Plan Chemotherapy	From permitted chemotherapy regimens
✓ Plan endocrine therapy (if pre-menopausal)	Do you intend to treat with AI or tamoxifen?
✓ Administer OPTIMA Patient Questionnaire Booklet	Quality of Life Health Resource Use questions
✓ Take medical history	Complete <i>Baseline Details Form (CRF 3)</i>

Randomisation process

WARWICK

CLINICAL TRIALS UNIT

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



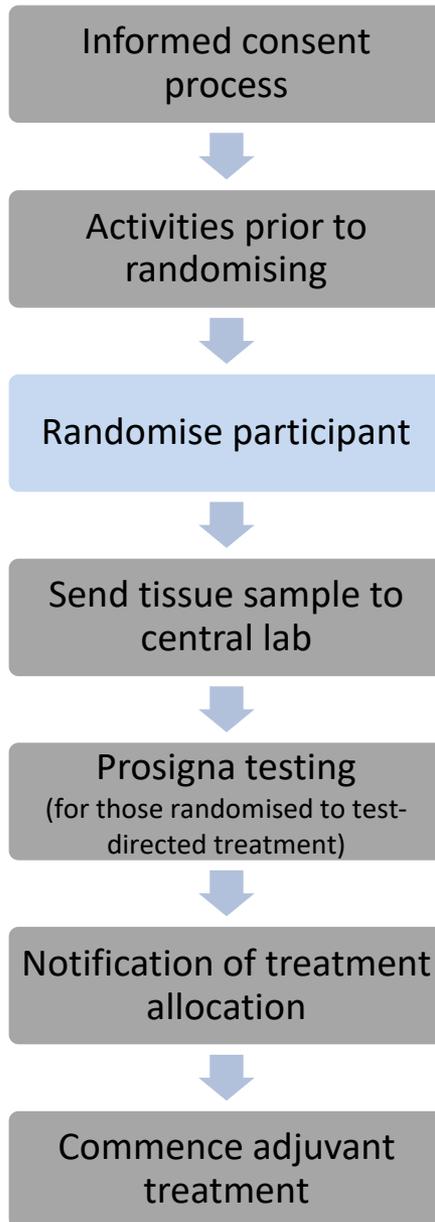
Notification of treatment allocation



Commence adjuvant treatment

- Telephone Warwick Clinical Trials Unit Randomisation Service.
 - *Telephone number found on the form and in the protocol*
- The Randomisation officer will ask you to confirm the information documented on the *Randomisation Form (CRF 2)*
- At the end of the call you will be given a 4 digit Participant Trial Number
 - *This is often referred to as a 'TNO'*

Randomisation form



Information required at randomisation:

- Site + participant details and confirmation of eligibility
- Type of consent given (Written vs Remote Verbal Consent)
 - When participant has given Remote Verbal Consent , CRF 2a must be completed prior to treatment allocation.
- Whether approached & consented for the Qualitative Recruitment Study
- Stratification variables
 - Tumour size
 - Number of involved nodes
 - Histological grade
 - Menopausal status
- Planned treatment
 - Intended chemotherapy regimen (a stratification variable)
 - If pre-menopausal, intent to treat with AI or tamoxifen

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Diagnostic tissue blocks

WARWICK

CLINICAL TRIALS UNIT

- Following randomisation a **tissue block should be sent within 3 working days.**
- Site pathologist selects a representative tissue block from the surgical resection (SOP provided).
- Site completes the Tissue Transit Form
 - Includes details of invasive tumour size and number of involved nodes; information included in Prosigna test result.
 - Must be completed by a trial investigator or pathologist who is a member of the breast MDT.
- Site transmits the Tissue Transit Form, and copies of all applicable anonymised histology reports, to the OPTIMA trial office.
- Site packages tissue block, include the Tissue Transit Form (retain a copy for site file), copies of applicable anonymised histology reports and send to the Central Laboratory. (Packaging provided and postage paid for by trial.)
- Email to site to confirm arrival of tissue block at central lab.

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Redaction

All pathology reports which are sent to the OPTIMA trial office and the central lab must be fully redacted of patient identifiable data (PID).

- Please make sure participant TNO and initials are written on each page
- Check there is no PID within the body of the report as well as header
- Un-redacted reports will be recorded as a protocol violation

Permitted data items

- Date of Birth – This is PID but required as source data for sample tracking and matching pathology reports and tissue transit forms to the correct patient
- Lab number – not PID

Must be redacted

- Participant Name, Address, Hospital Number, NHS Number

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Tumour Block Selection

If in doubt ask!

WARWICK

CLINICAL TRIALS UNIT

Patients who have received pre-operative endocrine treatment

- a pre-treatment core biopsy should be selected.
NOTE: A tumour block from a surgical excision or other on-treatment biopsy is not acceptable: treated tumours are likely to have a lower Prosigna Score which could affect treatment allocation.

Patients with a unifocal tumour

- a representative tumour block should be selected

Patients with multiple ipsilateral tumours

- Blocks from more than one lesion should be submitted when they are
 Considered clinically significant by the referring site and
 Interpreted as synchronous primary cancers

NOTE: Involved lymph nodes are not suitable for trial-specified laboratory investigation

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Non-luminal tumours

WARWICK

CLINICAL TRIALS UNIT

- Patients with non-luminal tumour subtypes identified by Prosigna testing will have central confirmation of receptor status.
- Most of these are expected to be high-score tumours correctly identified as ER positive & HER2 negative
- A few tumours will be ER negative/ low-positive or HER2 positive/amplified on re-testing.
- These tumours are ineligible - sites will be notified.
- Patients with ineligible tumours should be treated appropriately for the tumour characteristics.
- Patients remain in OPTIMA and will continue with trial follow-up.

Testing & treatment allocation

Informed consent process

Activities prior to randomising

Randomise participant

Send tissue sample to central lab

Prosigna testing
(for those randomised to test-directed treatment)

Notification of treatment allocation

Commence adjuvant treatment

TEST-DIRECTED ARM

- Central lab receives sample
- Sample assessed for invasive tumour content
- Prosigna test performed
- Prosigna test results reported to OPTIMA trial office
- OPTIMA trial office notify site of participant's treatment allocation

STANDARD/CONTROL ARM

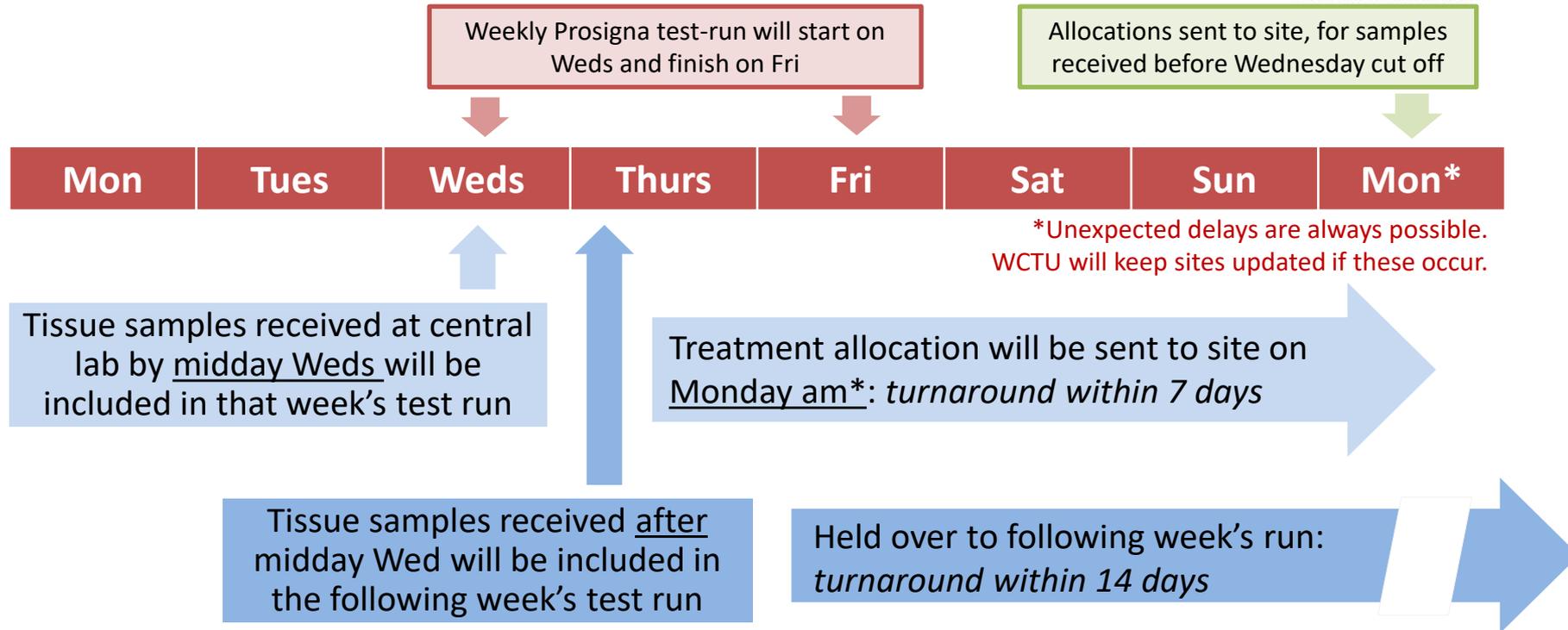
- Central lab receives sample
- Sample assessed for invasive tumour content
- Sample stored
- OPTIMA trial office notify site of participant's treatment allocation

TIME FROM RANDOMISATION TO NOTIFICATION OF TREATMENT ALLOCATION IS 2-3 WEEKS

For patients allocated to chemotherapy, randomisation is blinded from sites

Understanding the lab timetable

WARWICK



- Other factors that may impact the timeline:
 - Test failure (estimate 2%): repeat following week
 - Additional tests required (ER, HER2 confirmation for tumours with non-luminal Prosigna subtype, estimate 4%)
- Trial office will introduce balanced delays to notification of treatment allocation for control arm patients: you cannot assume a delay means that the patient is in the test-directed arm



Before treatment allocation

WARWICK

CLINICAL TRIALS UNIT

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

✓ Eligibility check	WCTU will check all paperwork and ensure that the patient meets the eligibility based on their tumour
✓ Block processing	HSL-AD will process the tumour block(s) and check all paperwork to ensure that the tumour is acceptable for OPTIMA
✓ Confirm consent	WCTU will confirm the type of consent received. Full written consent must be received before allocation can be released. Site should complete <i>Randomisation Form (CRF 2a)</i> prior to allocation, if required.

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

After treatment allocation

WARWICK

CLINICAL TRIALS UNIT

Once all checks have been completed, and all queries resolved, allocation will be processed by WCTU.

Allocations are automatically emailed to Site and can be sent to anyone on the Delegation log as required.

Allocations are always sent to:

- Randomising Investigator
- Person who made the Randomisation phone call
- Main Site Contact (as per the delegation log)

Tissue banking

- The OPTIMA team is committed to further research to develop and improve multi-parameter assays.
- Tissue blocks for all patients will be stored in the OPTIMA Tissue Bank.
- The stored tissue block will be returned on request in the event that the treating site needs it for diagnostic use.
- Prosigna testing on stored tumour samples from patients randomised to the control arm is planned to allow outcome analysis for patients with low-score tumours. This is very important information for clinicians.
- Intended research includes undertaking additional multi-parameter testing on stored samples to allow evaluation of these tests in predicting outcome.

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Surgery

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

Before Trial Entry:

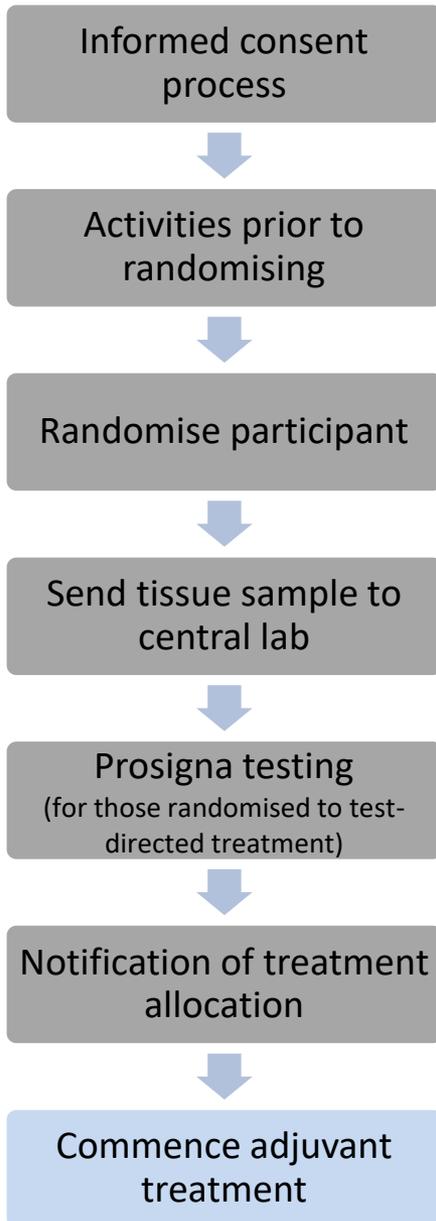
- Before trial entry appropriate surgery should be performed according to local guidelines
- All planned axillary surgery must be completed before trial entry

Following Trial Entry:

- Re-excision of margins or completion mastectomy permitted following trial entry

Chemotherapy

- Chosen from a list of permitted regimens.
- Intended regimen must be stated at randomisation.
- Chemotherapy is recommended to be started within 2 weeks of treatment allocation.
- Important to reassure the patient that waiting this amount of time will not have any detrimental effects on their health or outcome.
- Treatment and monitoring according to local guidelines.



PERMITTED REGIMENS	
✓ FEC75-80	✓ TC
✓ FEC90-100	✓ TAC
✓ EC90-100	✓ (F)EC-T
✓ E-CMF	✓ (F)EC-Pw/P2w
	✓ Dose dense AC/EC-P

Endocrine therapy

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

- Endocrine therapy is recommended to be started no later than:
 - 2 weeks from treatment allocation in patients assigned to no chemo
 - 4 weeks after day 1 of the final cycle of chemo for all other patients
- The endocrine therapy a participant is given is based on the patient's gender and for women their menopausal status at the time of trial entry (i.e. consent), not when hormone therapy is initiated.
- The recommended duration of endocrine therapy is 10 years for all patients.

Endocrine therapy

Initial treatment period (years 0-5)

Male:

- Tamoxifen

Postmenopausal at trial entry:

- Aromatase inhibitor. Tamoxifen may be given where there is a contraindication to aromatase inhibitor therapy.

Premenopausal at trial entry:

- Tamoxifen or an aromatase inhibitor. (Investigators must declare treatment intent at randomisation.)
- Participants should also undergo ovarian suppression e.g. with a Gonadotropin-releasing hormone (GnRH) agonist.

Informed consent process

Activities prior to randomising

Randomise participant

Send tissue sample to central lab

Prosigna testing
(for those randomised to test-directed treatment)

Notification of treatment allocation

Commence adjuvant treatment

Ovarian Suppression

Informed consent process

Activities prior to randomising

Randomise participant

Send tissue sample to central lab

Prosigna testing
(for those randomised to test-directed treatment)

Notification of treatment allocation

Commence adjuvant treatment

All women who are pre-menopausal at trial entry should be treated with ovarian suppression for at least 3 years

- Optimal treatment
- Ensures balance between trial arms.

Treatment options:

- Licensed GnRH agonist, such as goserelin 3.6mg s.c. monthly or leuprorelin acetate 11.25mg s.c. 3-monthly for at least 3 years.
N.B. refer to protocol guidance for monitoring GnRH agonist & AI combination
- Bilateral surgical oophorectomy
Radiation menopause is not permitted.

Deferred initiation of GnRH agonists:

- Post chemotherapy amenorrhoea is common in older women. In many but not all cases this will be permanent.
- GnRH agonist treatment may be deferred for patients with amenorrhoea but should be initiated in the event of resumption of menses up to 2 years from trial entry

Endocrine therapy

Extended treatment period (years 6-10)

As the OPTIMA population is considered to be at high risk of late relapse, all patients are advised extended adjuvant endocrine therapy for a further 5 years to a total of 10 years as follows:

Male: Tamoxifen

Female: Aromatase inhibitor or tamoxifen

For women who were deemed premenopausal at trial entry, if considering switching from tamoxifen to an aromatase inhibitor at 5 years, the patient's menopausal status needs to be confirmed at this stage as postmenopausal.

There is detailed guidance in the protocol regarding the determination of menopausal status in women receiving anti-oestrogen treatment.

Informed consent process

Activities prior to randomising

Randomise participant

Send tissue sample to central lab

Prosigna testing
(for those randomised to test-directed treatment)

Notification of treatment allocation

Commence adjuvant treatment

Adjuvant bisphosphonates

WARWICK

CLINICAL TRIALS UNIT

Informed consent process



Activities prior to randomising



Randomise participant



Send tissue sample to central lab



Prosigna testing
(for those randomised to test-directed treatment)



Notification of treatment allocation



Commence adjuvant treatment

- Adjuvant bisphosphonate treatment is associated with a survival benefit.
- Benefit seen in postmenopausal women and those who become postmenopausal as a result of their treatment.
- All OPTIMA patients are eligible for treatment with a bisphosphonate (*either postmenopausal at trial entry or treated with ovarian suppression if pre-menopausal*).
- It is recommended that patients in the OPTIMA trial receive bisphosphonate treatment (oral or intravenous) for 2-5 years according to NICE guidelines.
- To avoid potential treatment imbalance, sites should ensure bisphosphonate treatment is the same for all patients irrespective of treatment allocation (i.e. whether the patient is receiving chemotherapy or not).

Follow-up

- Annual follow-up to 10 years
- Annual Follow-up Case Report Form to be completed
- Follow-up can be carried out in clinic.
- Telephone follow-up is permitted for patients who have been discharged from clinical review.
- Follow-up by e-mail is permitted if this is permitted by site's local information governance policies.
- At 12 and 24 months administer OPTIMA Patient Questionnaire Booklet.



QoL and health resource use

WARWICK

CLINICAL TRIALS UNIT

- Patient Questionnaire data is key to the outcomes of OPTIMA in terms of patient acceptability (QoL data) and cost effectiveness (health resource use)
- QoL and health resource use data is collected via Patient Questionnaire Booklets which are completed at the following time-points:
 - Baseline
 - 3 months after trial entry
 - 6 months after trial entry
 - 12 months after trial entry
 - 24 months after trial entry

At all time-points except baseline can be completed either in clinic, by post or telephone if not standard practice to see patient in clinic at this time point.

**Trial entry defined as date of informed consent*

Patient withdrawal

- Patients can withdraw from the trial at any time
- Withdrawal of patients should be communicated to the OPTIMA Trial Office as soon as possible and a Withdrawal CRF completed.
- Patients who move away from the area should not automatically be withdrawn from the trial. Transfer to another site or telephone follow-up is permitted.
- If a patient declines to follow their trial allocated treatment or ceases treatment early, this patient should not be withdrawn. Treatment, follow-up and quality of life data should be collected unless patient explicitly forbids further data from being collected.

Compatible Trials

Patients randomised into OPTIMA can also take part in the following trials:

- POETIC-A (patients treated with pre-operative AI in the registration phase who do not proceed to randomisation are eligible)
- Add-Aspirin
- POSNOC (N.B. all planned axillary surgery must be completed prior to randomisation into OPTIMA)
- Radiotherapy trials
- Non-randomised trials

- Please check with the trial office if you are in doubt. In general anything that does not involve drug treatment is allowed

PI responsibilities

- For the conduct of the trial at their site.
- To nominate appropriately experienced staff to assist in the recruitment and follow-up of participants.
- To maintain a Site Signature and Delegation Log documenting the roles and responsibilities of site staff.
- Make sure Good Clinical Practice (GCP) training for all staff is up to date
- To conduct of the trial in compliance with the protocol.
- To document and explain any deviation from the protocol.
- For all trial-related medical decisions.
- To ensure informed consent is obtained and documented according to GCP.
- Ensure accuracy, completeness, legibility and timeliness of the data reported on CRFs.
- Maintenance of Investigator Site File.
- Provisions for archiving essential documents.
- PLEASE NOTE: No expedited SAE reporting for OPTIMA

The OPTIMA Challenge

WARWICK

CLINICAL TRIALS UNIT

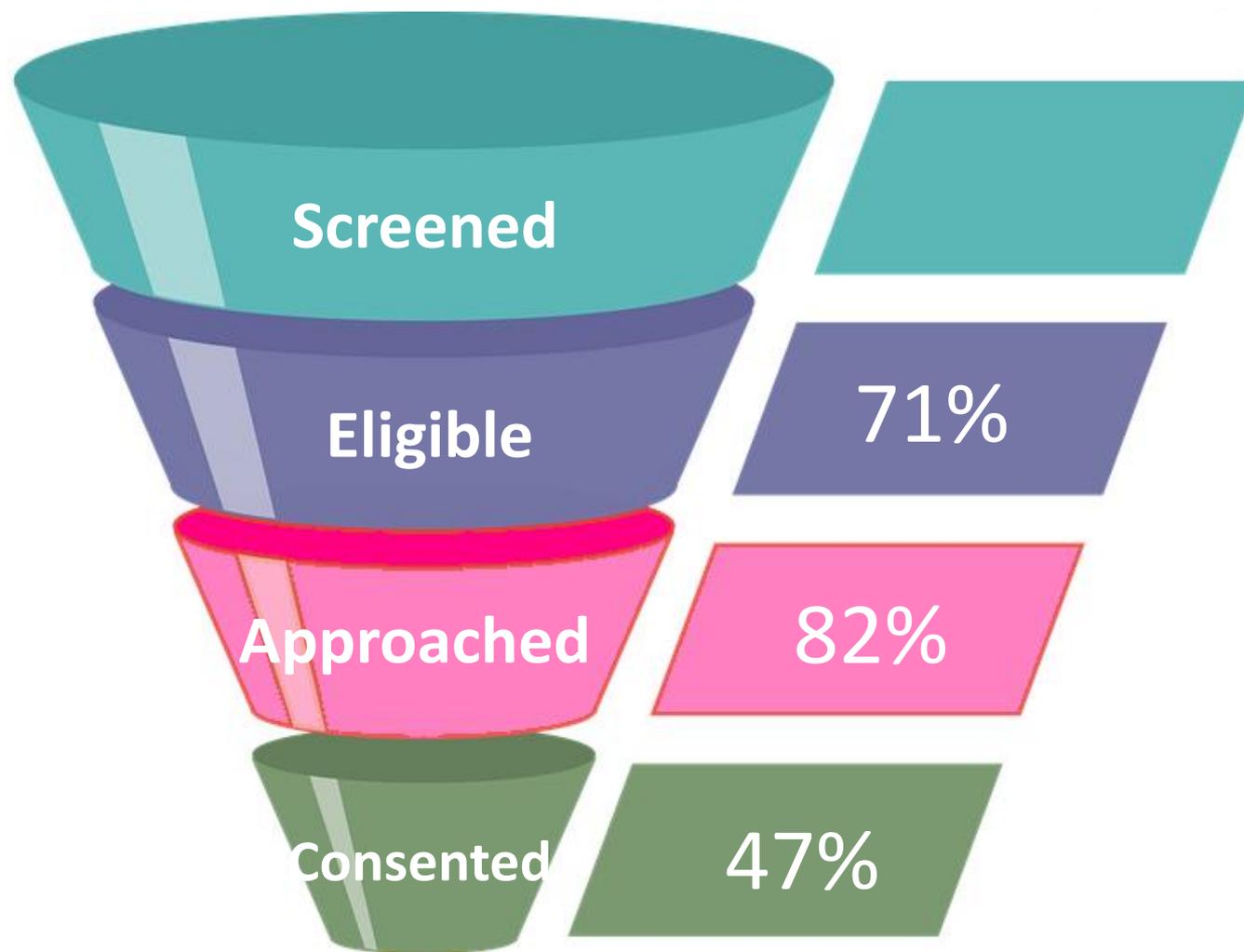
- OPTIMA offers the only chance of generating robust evidence for the chemotherapy predictive hypothesis.
- OPTIMA needs to recruit 4500 patients over 5 years to answer the question
 - Non-inferiority trials need to recruit a lot of patients
- To achieve this, sites need to recruit at least 1 patient per month
- Most sites need to offer OPTIMA to at least 2 patients per month
 - Not everybody asked will join OPTIMA.



Image courtesy of UCL Health Creatives

Screening and Recruitment

WARWICK



Screening data for Jan 2019 - June 2020

Recruiting to all RCTs can be challenging...



Recruitment lower/ slower than expected

Recruiting to all RCTs can be challenging...



Recruitment lower/ slower than expected

WARWICK

CLINICAL TRIALS UNIT

- **Disrupts routine practice**
- **Relies on unusual concepts**
- **Alters Dr/patient relationship**

Qualitative Recruitment Study (QRS)



What we'd like you to do

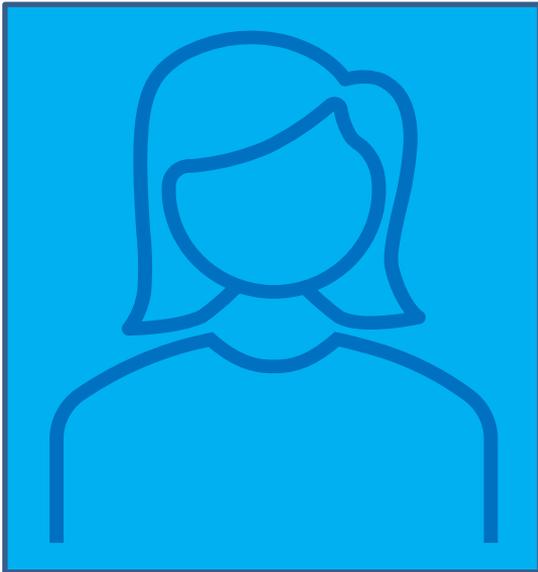
All sites

- Facilitate patient interviews
- Keep screening logs up to date

Some sites

- Participate in an interview
- Audio-record OPTIMA recruitment appointments

QRS Patient Interviews



Insight into patient decision

Patients that decline ✓

Patients that accept ✓

Your role:

After the patient has made a decision about OPTIMA:

- Seek consent to pass on patient contact details to QRS researcher
- Register consent for patient details to be passed to the QRS researcher
- Pass on contact details to QRS researcher.

QRS Audio-recordings

- We'll provide a small audio-recorder and clear instructions
- Patients generally comfortable with recording
- What happens to the recordings?
- Making use of the data
 - share examples of what seems to work well
 - collaboratively work through challenges
- Recordings are confidential and quotes are anonymised





- COVID-19 and OPTIMA
- Essential Documents
- Newsletters
- Administering OPTIMA
- Qualitative Recruitment Study
- Recruiter training and support
- Publications
- OPTIMA Governance

Qualitative Recruitment Study

To support recruitment, the OPTIMA study contains a Qualitative Recruitment Study (QRS). The QRS aims to understand the sources of recruitment difficulty, as the study is underway and using these insights, develop strategies to address recruitment challenges throughout the remainder of recruitment.

QRS activities

Phase I: Understanding recruitment obstacles

- Mapping recruitment pathways, assessing screening and eligibility procedures
- Interviews with trial staff and sometimes patients
- Audio-recordings of 'recruitment consultations'

For information about audio-recording and patient interviews & current forms:
optimabreaststudy.com

carmel.conefrey@bristol.ac.uk

nicola.farrar@bristol.ac.uk

Research staff involvement is minimal, all we need you to do is ask the patient if they'd be prepared to be contacted by a researcher from the QuinteT team about a possible interview. The procedure for approaching and registering patients is in QRS [Patient Interview Procedure Note](#).

Essential QRS documents

- [Staff information sheet and consent form V4.0 2018-11-08](#)
- [QRS Verbal Consent Form V2.1.27 Sep 2016](#)
- [OPTIMA QRS Patient IS V3.0 2018-11-08](#)
- [OPTIMA QRS Patient CF audio-recording consultations V4.0 2018-11-08](#)
- [OPTIMA QRS Patient Interview Contact Details Form V4.0 2018-11-08](#)
- [OPTIMA QRS Patient Interview Contact Details Form V4.0 2018-11-08](#)
- [QRS Patient Registration Form v2 015 apr 2019](#)
- [Patient Interview Procedure Note V1 2020-06-29](#)
- [QRS Audio-recording patient interview procedure V5 2020-07-15](#)

Recruitment Tips

Cultivate a united team approach

WARWICK

CLINICAL TRIALS UNIT



Essential for:

- Identifying eligible patients
- Preparing patients for OPTIMA discussion – consistent message

Patients will have established trust in their surgeon and breast care nurse and what they say.

Top tip:

Agree who is going to say what and when to patients about adjuvant chemotherapy and OPTIMA

Preparing the team

The OPTIMA Guide for Surgeons

Surgeons and the OPTIMA study
Surgical support for OPTIMA at the multidisciplinary team meeting is key for identifying potentially eligible patients. Whilst oncologists discuss OPTIMA in detail and consent patients, what a surgeon says to a patient about adjuvant chemotherapy is extremely important as it creates expectations. As such, surgeons set the scene for OPTIMA recruitment.

This guide summarises the study and its surgical considerations and offers tips for preparing eligible patients for a discussion about OPTIMA.

The study
OPTIMA is a randomised clinical trial designed to validate the use of tumour gene multi-parameter tests to guide chemotherapy use for patients with ER-positive HER2-negative early breast cancer. OPTIMA uses the Prosigna (PAM50) test but the design allows other tests to be evaluated.

The trial has two underlying assumptions

1. Multi-parameter tests all predict chemotherapy
2. Tumour stage is prognostic for all patients

Patients with more advanced stage are therefore unlikely to benefit from chemotherapy if the tumour has a low test score despite an unfavourable prognosis.

The trial population are patients who would ordinarily be treated with chemotherapy. OPTIMA randomises eligible participants between standard treatment (chemotherapy followed by endocrine therapy) or to have a Prosigna test performed on the tumour. If the tumour has a high Prosigna score (>60) then the patient will be assigned to standard treatment whilst those with a lower score receive endocrine therapy only. Patients receiving chemotherapy are blinded to the endocrine therapy as they are randomised to control arm or high Prosigna test (randomised to control arm or high Prosigna test score). An estimated two thirds of patients whose tumours are tested will avoid chemotherapy.

The Prosigna test is performed on fixed tissue in a UK-based lab. The test takes less than 2 weeks from consent for the majority of patients. See the diagram overleaf for more information on study design.

OPTIMA is a pragmatic study that tries to accommodate local practice and not dictate treatment. In principle OPTIMA participants can join other clinical studies. This includes POSNOC.

OPTIMA expects to recruit mostly patients with node-positive (including micrometastatic) disease but does allow node-negative patients if for any reason multiparameter testing (e.g. with Oncotype DX) is not used as standard of care.

Surgical considerations*
OPTIMA is an adjuvant trial, neoadjuvant treatment is not permitted. This includes endocrine therapy as this reduces the score of all multi-parameter tests. Secondary breast surgery such as re-excision of margins or secondary mastectomy is permitted following treatment initiation including chemotherapy but all planned axillary surgery must be completed prior to a trial stratification factor. Axillary node status is a trial stratification factor. Axillary radiotherapy as an alternative to clearance is allowed and should take place following chemotherapy (if the patient is allocated to this).

Short term adjuvant endocrine therapy may be given pre-randomisation but the time limit for patients to join OPTIMA is 8 weeks following their final surgery.

* Rules on neoadjuvant endocrine therapy and time limit for joining the study will be relaxed in protocol version 6.

Talking with patients about OPTIMA
When preparing patients for an oncology appointment it would be helpful to flag up that part of that conversation will include a discussion about a clinical study – OPTIMA. Here is a suggestion for how you might do this:

"The oncologist will talk with you about further treatment. This will include a conversation about a study (called OPTIMA) to see whether you're likely to benefit from chemotherapy, as not all patients do."

The OPTIMA Guide for Breast Nurse Specialists

Breast Nurse Specialists and OPTIMA
OPTIMA is a randomised controlled trial designed to find out if a multi-parameter test can effectively and safely identify if a patient is likely to benefit from adjuvant chemotherapy or not. OPTIMA uses the Prosigna test.

Recruitment to OPTIMA is a team activity relying on surgeons, breast nurse specialists, pathologists, oncologists, research nurses and trial co-ordinators.

Breast nurse specialists build trusting relationships with patients and often patients will look to them for guidance about what will happen following surgery. What you and your surgical colleagues say to a patient about adjuvant treatment, can shape patient expectations and in turn, recruitment to OPTIMA.

This guide summarises the study and offers tips for preparing eligible patients for a discussion about OPTIMA.

The Study
OPTIMA aims to identify patients most likely to benefit from chemotherapy and those who may be better treated by moving directly to hormone therapy.

OPTIMA expects to recruit mostly patients with node-positive (including micrometastatic) disease because negative patients can participate if Oncotype DX or other tests are not used.

Multi-Disciplinary Teams will identify patients with ER-positive HER2-negative early breast cancer that would ordinarily be treated with chemotherapy and explain the study to eligible patients and invite them to join OPTIMA.

OPTIMA randomises eligible participants between standard treatment (chemotherapy followed by endocrine therapy) or to have a Prosigna test performed on the tumour. If the tumour has a high Prosigna Score (>60) then the patient will be assigned to standard treatment whilst those with a lower score receive endocrine therapy only. Patients receiving chemotherapy are blinded to the endocrine therapy as they are randomised to control arm or high Prosigna test (randomised to control arm or high Prosigna test score). An estimated two thirds of patients whose tumours are tested will avoid chemotherapy.

The Prosigna test is performed on fixed tissue in a UK-based lab. The test takes less than 2 weeks from consent for the majority of patients. See the diagram overleaf for more information on study design.

Introducing OPTIMA to Patients
When preparing patients for an oncology appointment it would be helpful to flag up that part of that conversation will include a discussion about a clinical study – OPTIMA. Here is a suggestion for how you might do this:

"The oncologist will talk with you about further treatment. This will include a conversation about a study (called OPTIMA) to see whether you're likely to benefit from chemotherapy, as not all patients do."

Please avoid presenting chemotherapy as a definite as this can create an expectation of treatment. It may then be difficult for the oncologist to introduce the study concept and the idea that they may not get chemotherapy.

OPTIMA Patient Information Flyer
Have you just had surgery for breast cancer? You might be suitable for OPTIMA.

Working with patients, the OPTIMA team have produced a patient information flyer to introduce and prepare patients for a fuller discussion with an oncologist about OPTIMA. The flyer is in addition to the patient information sheet.

We ask that you hand it out at post-surgical appointments to patients flagged by the MDT as potentially eligible for OPTIMA.

Preparing the Patient

WARWICK

CLINICAL TRIALS UNIT



Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it

NHS



- Mention OPTIMA early on
- Large international study – 111+ centres across UK and Norway
 - NHS funding body (NIHR) – important question to NHS
 - ***Part of something big!***

Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it
2. Lead on benefit of hormone therapy and contrast with uncertainty of chemotherapy benefit for all patients

“You are definitely somebody who would benefit from hormone treatment, and that’s likely to be one of the most important parts of your treatment. But what is much more difficult to know is whether you would benefit from chemotherapy as well.”

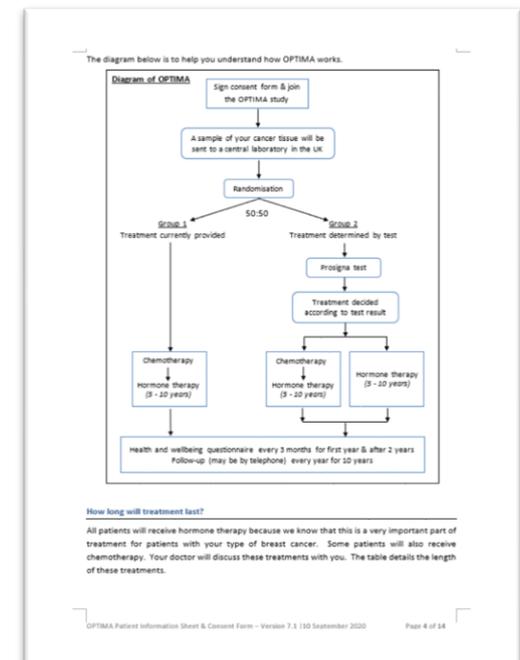
Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it
2. Lead on benefit of hormone therapy and contrast with uncertainty of chemotherapy benefit for all patients
3. Give the rationale for OPTIMA – improve decision making to better target the use of chemotherapy

“We know it’s a hormone sensitive cancer because we do a test on the tumour that says it’s hormone sensitive [...] What we would really like to have is a test [...] to see if it’s a chemo-sensitive tumour- because not all tumours are.”

Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it
2. Lead on benefit of hormone therapy and contrast with uncertainty of chemotherapy benefit for all patients
3. Give the rationale for OPTIMA -
4. Run through what happens when a patient joins the study, many find the diagram in the PIS a helpful tool.



Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it
2. Lead on benefit of hormone therapy and contrast with uncertainty of chemotherapy benefit for all patients
3. Give the rationale for OPTIMA -
4. Set out what happens when a patient joins the study – many find the diagram in the PIS a helpful tool
5. Be clear about what is being randomised i.e.
chemotherapy as SoC v test directed chemotherapy
(the patient **is not being randomised** to chemotherapy v no chemotherapy)

Tips for Discussing OPTIMA

1. Mention OPTIMA early on – can then return to it
2. Lead on benefit of hormone therapy and contrast with uncertainty of chemotherapy benefit for all patients
3. Give the rationale for OPTIMA -
4. Set out what happens when a patient joins the study – many find the diagram in the PIS a helpful tool
5. Be clear about what is being randomised i.e. to have chemotherapy as SoC or test directed (the patient is not being randomised to chemotherapy v no chemotherapy)
6. Say and show that you are happy for the patient to join the study and have their treatment determined by it.

“I’m very happy for you to enter the study and to follow the treatment that you would get given, whatever that may be.”

7. Engage with Patient Preferences

- What sounds like a preference, can be based on misconceptions, not having full info...



Everyone I know that's survived (breast cancer) has had chemotherapy. To me, my brain's telling me that's obviously a good thing.

Everybody has to have chemotherapy anyway, don't they?

- Recruiter's role is to:
 - Elicit concerns and preferences
 - Address misconceptions
 - Provide information to 'complete the picture'
 - Explore reasons for preference

Strengthening informed consent whatever the decision

Support for Recruiters

OPTIMA tips for recruiters, April 2018

This document provides suggestions for recruiters involved in the OPTIMA study. These tips are based on the audio-recordings of consultations made by investigators recruiting to OPTIMA around the UK. Please consider using some of these suggestions to complement your own consultation style and approach. It can be helpful to think of the recruitment consultation in three stages: opening, middle and closing.

Opening

- Introduce the OPTIMA study to eligible patients early in the consultation. e.g.:
 - "Hospital name) is taking part in a national NHS clinical study called 'OPTIMA', which I'd like to talk through today, as it relates to what kind of treatment we will consider after surgery."
- Establish that following surgery, further treatment is recommended to reduce the risk of cancer returning either in the breast or elsewhere.
- Explain that there are different types of breast cancer. The type of treatment given after surgery depends on the type of breast cancer.
- Start off with the 'certainties' – the treatments that we KNOW will benefit the patient: hormone therapy (and the type of breast cancer).
- Explain that there is less certainty about which patients should receive chemotherapy, because not all tumours are 'chemotherapy sensitive'. Up until now, we have not had the technology to determine which tumours are likely to respond to chemotherapy, and which will not.

"We know it's a hormone sensitive cancer because we do a test on the tumour that says it's hormone sensitive. What we'd really like to have is a test to see if it's a chemo-sensitive tumour - because not all tumours are."

Middle

Talking about the Prosigna test

- Introduce Prosigna and explain it is a test that may be able to predict who would benefit from chemotherapy. Patients can become fixated on population level prognostic calculations, and often assume that this equates to definitive benefits for them. This then makes it difficult to understand the basis of the OPTIMA study, which looks towards making more refined, personalised decisions about the likelihood of chemotherapy benefit based on the biology of the tumour removed. Worth remembering that Prosigna gives more reliable information than histopathological grade.

OPTIMA recruiter tips: Engaging with patient preferences

Patient preferences are often cited as an obstacle to recruitment. Drawing on audio-recordings and interviews as part of the OPTIMA Qualitative Recruitment Study (QRS), this tips document takes a look at how patients come to have a preference and offers strategies for exploring and responding to these.

How do patients develop preferences?

Websites, social media, friends and family, and your fellow colleagues all have the potential to shape what a patient thinks about adjuvant treatment and OPTIMA.

What can you do about this?

Starting with your colleagues, please ensure your surgeon, breast nurse specialist and radiography colleagues are familiar with OPTIMA. When talking with patients about treatment following surgery, ask them to:

- Encourage patients to keep an open mind about follow-on treatment
- Introduce uncertainty of chemotherapy benefit for all
- Prepare patients for a discussion about OPTIMA with their oncologist

To help, we've produced an OPTIMA guide for surgeons and one for breast nurse specialists and a 2-sided patient information flyer for your colleagues to hand to patients at the post-surgery appointment. All are available from the OPTIMA team at Warwick (optima@warwick.ac.uk).

Following on to your response – OPTIMA is a treatment de-escalation study with very different treatment arms. It is not surprising that some patients may have a strong initial reaction when the trial is presented to them. To engage with this initial response by inviting the patient to share with you what's behind their reaction.

We appreciate that engaging with preferences may be a little different to what you would normally do but in the context of recruiting to a study, it leads to better informed consent whatever the final decision. To help with this conversation, we share some strategies that have worked well for many recruiters.

Strategies for engaging with preferences

Acknowledge the preference and open up the discussion	<ul style="list-style-type: none"> "OK. I'd like to go through all your options, to make sure you have all the relevant information..." (if at the beginning of the conversation) "Keep an open mind as I recap all your options..."
Explore patient's rationale	<ul style="list-style-type: none"> "What is it that worries you about X?" "Are you concerned about X? Perhaps I can relieve some of those concerns?"
Address patient's views, and respond to their specific concern	<ul style="list-style-type: none"> Offer reassurance Fill information gaps Address misconceptions

Recruitment and Informed Consent Guidance – Patient Preferences Version 1.0, June 2019 Page 1 of 2

Newsletter November 2018

Optimal Personalised Treatment of early breast cancer using Multi-parameter Analysis

Recruitment update: 1126
OPTIMA prelim – 412 OPTIMA main – 714

October has been another good month, we exceeded our target with an excellent 56 patients randomised! Congratulations to joint top recruiters: **Boston Oncology Centre** and **Royal Devon and Exeter Hospital** – 4 patients each.

We know how hard you are working to screen and recruit eligible patients, please keep going!

Legoblocks

If you are sending a legoblock please make sure that they are posted later than Monday to be included in the Wednesday Prosigna test.

One reason for this is that occasionally legoblocks need to be re-embedded before processing for OPTIMA.

Recruitment tip of the month - Lead with treatment 'certainties'

It falls to lead on adjuvant treatments that are certain...
"There are a couple of treatments that you should definitely have, one of which is radiotherapy to the breast... The second thing you should definitely have is some hormone based tablets."

This approach provides a platform to contrast the 'certainties' of some treatments with the uncertainties of chemotherapy benefit for all patients, and in therapy use.

OPTIMA Stratification Variables

Within OPTIMA, we stratify by the following variables:

- Chemotherapy regimen
- Number of involved nodes
- Histological grade
- Tumour size
- Menopausal status

Additional information is recorded on the Randomization CRF (Form 1).

These data items are **critical** for the outcome of the trial so please ensure that these items are accurate before you randomise the patient.

New team member

Welcome to Adam Raynes who has joined the Warwick OPTIMA team as a **Study Coordinator**.

Consent Forms

Please note that completed consent forms should **not** be sent to the OPTIMA trial office.

A copy should be given to the patient, one for the patient's hospital records and store the originals in section 8.3 of your Investigator Site File.

Any consent forms received here will, unfortunately, constitute a protocol violation.

Redaction

When redacting histology reports to send to the trials office and the lab, please also remove the name of the person who requested the report. Thank you!

OPTIMA Audio-recording

If you have a recorder, please ask your next eligible patient if you can record the appointment. Contact carmel.consefrey@bristol.ac.uk for more information.

Contact Us
OPTIMA trial office 02476 150948 optima@warwick.ac.uk

- OPTIMA Tips for recruiters – kept under review
- Monthly recruitment tip in OPTIMA Newsletter

Here to support you recruit to OPTIMA



Carmel.Conefrey@bristol.ac.uk
Optimabreaststudy.com

The screenshot shows the OPTIMA website interface. The header includes the OPTIMA logo and navigation links: 'Taking Part in OPTIMA', 'OPTIMA Recruiting Sites', 'The OPTIMA Team', and 'Contact Us'. The main content area is titled 'Recruiter training and support' and contains a list of documents. The document 'Recruiter training and support' is highlighted with a red circle. Below the list, there are sections for 'Training and support documents' and 'Lunch with OPTIMA slides', each with a bulleted list of specific documents and dates. The footer contains copyright information for OPTIMA and the ABS Breast Surgery logo.

optima
Optimal Personalized Treatment of early breast cancer using Multi-parameter Analysis

Taking Part in OPTIMA | OPTIMA Recruiting Sites | The OPTIMA Team | Contact Us

COVID-19 and OPTIMA
Essential Documents
Newsletters
Administering OPTIMA
Qualitative Recruitment Study
Recruiter training and support
Publications
OPTIMA Governance

Recruiter training and support

Drawing on the Qualitative Recruitment Study we've developed a number of documents to support staff to recruit to OPTIMA.

Training and support documents

- OPTIMA Remote Consent Procedure v1.0 2020 10 02
- OPTIMA Recruitment and informed Consent Guidance V2.0 2018 03 28
- OPTIMA Recruiter 1 on 1 Language With Patient Preferences FINAL 2019 04 12
- The OPTIMA guide for surgeons FINAL v1.0 2018 08 16
- The OPTIMA Guide for Breast Nurse Specialists Final Version 1 2018 08 16

Lunch with OPTIMA slides

- Lunch with OPTIMA - COVID19 update (presented 2020 08 18, 2020 09 24)
- Lunch with OPTIMA - Protocol v7.0 update (presented 2020 10 07, 2020 11 03)

© 2020 OPTIMA

The OPTIMA Study is funded by National Institute for Health Research (NIHR) Programme Grant reference 10261063. The information contained in this website is for general information about the OPTIMA study and is provided by the University of Warwick, Cancer Trials Unit & University College London. The views expressed are those of the author(s) and are not necessarily those of NIHR or the Department of Health and Social Care or representatives of the views of the funder, sponsor or other participating organisations. Trial Registration Number ISRCTN12004492

ABS
BREAST SURGERY

Screening log

- Include all patients identified as potentially eligible (ER+ve, HER2 –ve, suitable for adjuvant chemotherapy)
- Do not include those offered multi-parameter testing as standard of care
- Provides valuable insight into recruitment process and can highlight potential obstacles
- Requirement of reporting randomised controlled trials and part of GCP
- Requested monthly



OPTIMA Patient Screening Log

Site: _____ Principal Investigator: _____ Page: 1

Please include information for **ALL** patients identified by the MDT as **potentially eligible as thought to have ER positive and HER2 negative disease and would ordinarily be offered adjuvant chemotherapy**, except for those who are offered multi-parameter testing (e.g. Oncotype DX) as standard of care. The screening log will be requested on a monthly basis (please fax to 02476 151586 or email to optima@warwick.ac.uk).

Screening no.	Initials	Date screening initiated (d/m/yr)	Age (yrs)	No. involved nodes	Tumour size (mm)	Tumour grade	Is the patient eligible? (please circle)	Is the eligible patient approached? (please circle)	Did patient consent to be randomised into OPTIMA? (please circle)	Did patient consent to Qualitative Recruitment Study? (please circle)	Trial No. OR QRS Registration No.
OM1							Yes	Yes	Yes	Audio-recording Yes / No Interview Yes / No	
							No, why not? ¹	No, why not?	No, why not? ²		
OM2							Yes	Yes	Yes	Audio-recording Yes / No Interview Yes / No	
							No, why not? ¹	No, why not?	No, why not? ²		

Data collection

CRF completion

- ALL questions should be completed unless the question directs you not to.
- If data is missing please explain by means of a statement such as “not done”, “not applicable” or “unknown” so we do not query it as missing data.
- Please send original forms to be sent to the trial office and retain a copy for the site file.
- If you are not sure how to fill in any element of the form, we are very happy to help – call us anytime and we will be able to point you in the right direction.

Schedule of CRF return

- We ask for most of the CRFs to be sent to us within 4 weeks of completion.
- E.g. Baseline Forms to be sent within 4 weeks of randomisation.

Surgery CRF

- Asks you to attach the histology reports from surgery. Please obscure any identifiers and add participant’s trial ID.

Data collection

Data clarification process & CRF return

- Once a month send report to nominated person(s) by email.
- These list CRFs we would have expected to receive & any data queries.
- If treatment has been delayed or data manager on leave etc. please just let us know.
- We usually request a response to data queries within 2-3 weeks.

Self Evident Corrections

- We operate a system of self evident corrections on CRFs to limit the number of queries.
- All PI's and sites will be supplied with a list for approval
- All self evident corrections will be approved initially by the Trial Coordinator, all corrections will be made on the trial office copy of the CRF in green pen, and initialled and dated. We will not go back to site with these queries as the resolutions are self evident.
- *Example: Question asks if the patient has any previous or current diseases other than breast cancer and you have not ticked 'Yes' but there are diseases listed – we will tick 'Yes' with our initial and date. We will not go back to site with these queries as they are self evident.*

When can we activate your site?

Essential documents required before patients can be recruited:



- ✓ Trust R&D approval/ confirmation of capacity and capability
- ✓ Signed Site Agreement (CTA)
- ✓ Completed Site Signature & Delegation Log
- ✓ Principal Investigator's CV & evidence of GCP training
- ✓ Site initiation attendance log
- ✓ Signature to confirm local lab adheres to NEQAS standards
- ✓ Written confirmation of site activation/opening from the Trial Coordinator

OPTIMA team contacts

Please do not hesitate to contact us with any queries:

optima@warwick.ac.uk

WARWICK

CLINICAL TRIALS UNIT

Georgi Dotchin

OPTIMA Trial Manager
Tel: 02476 151 057

Katie McGuinness

OPTIMA Trial Manager
Tel: 02476 151 057

Lysbeth Evans

OPTIMA Trial Co-ordinator

Matthew Dalby

OPTIMA Trial Administrator

Michelle Davitt

OPTIMA Data Entry Clerk

Sam Careless

OPTIMA Data Entry Clerk

Carmel Conefrey

OPTIMA Qualitative Researcher
Tel: 0117 9287296

Email: carmel.conefrey@bristol.ac.uk